IMMUNOLOGY PRESENTATION AT THE 1990 NASA/NSF ANTARCTICA BIOMEDICAL SCIENCE WORKING GROUP

Richard T. Meehan, M.D.
University of Colorado Health Sciences Center

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A review of prior space immunology studies and relevant stress immunology studies were presented. In order to determine the unique effects of the space flight environment, including microgravity and novel types of ionizing radiation on human immune function, it will be necessary to define those changes which can be accounted for exclusively by the stresses associated with landing. This is especially important, since only one inflight experiment with an appropriate 1-G centrifuge has been performed to date.

An overview of methodology used for determining human in vitro lymphocyte activation, proliferation and effector cell function was presented and results of previous manned space flight immunology studies from Apollo through Shuttle were reviewed (1,2). Until the Shuttle era, lymphocyte assays were not very sensitive and had such large variations among normal subjects that it was difficult to define a consistent effect of space flight. More sensitive assay, however, even with Shuttle missions as brief as 6 days indicate depressed T-cell proliferative responses are routinely observed following space flight. Using a slight modification of the Shuttle assay, five different human stress-immunology models have been studied over the last 6 years in our lab. These have included: academic examinations of medical students having blood drawn during major test periods on three separate groups of first year students and two hypoxia studies (at 25,000 feet in a 6 week chamber ascent to the equivalent of Mount Everest and twice on Pikes Peak at 14,000 feet). These studies are particularly pertinent to Antarctica, since the altitude equivalent of 11,000 feet at the South Pole may affect some of the variables that are being measured in immunology, physiology or cognitive studies. An extravehicular study was performed drawing blood from 35 individuals before and immediately following a chamber exposure study (3). Preliminary results from 30 Shuttle astronauts investigated immunophenotype analysis and the role of a novel monocyte population in modulating the previously observed suppressed in vitro immune function (4). The results of the Air Force Academy cadet stress study were also presented.

Summary of Operation Everest II

An approximately 30% reduction in mitogenic proliferative responses were noted at 72 hours as was previously observed from Shuttle crews and this defect could also be observed in the first 24 hours of culture by measuring protein synthesis (5). In contrast, interferon production in the supernatants was extremely variable and therefore large numbers of subjects would be required to detect a uniform change in cytokine assays. B-cell function was completely unimpaired as measured by in vitro immunoglobulin product and nasal wash IgA levels. Serum IgM and IgA levels were actually increased in the plasma after 4 weeks of altitude exposure. This may be the result of depressed T-cell function. NK activity despite cytokine augmentation at 3 different effector: target ratios was unaffected. No changes were observed among T-cell helper: suppressor ratios by immunophenotyping, or B-cells whereas an increase in the percentage of monocytes was

observed. These results are consistent with previous human altitude studies by the Soviets which also show impaired T-cell function whereas B-cell function was unimpaired.

Summary of Medical Student Academic Stress Studies

Subject selection was crucial since less stress was observed in subsequent years when the method of recruitment did not induce as many reluctant students to participate. There was a trend ($P<.05$) of subjects with an increasing number of URIs to have lower in vitro T-cell proliferative responses. We also noted that females rated themselves as perceiving more stress during both control and test periods, emphasizing the importance of gender differences in these studies. The greatest change in stress-induced proliferative responses were observed when monocytes increased as they did during Operation Everest II, whereas cytokine production IL-2, and gama interferon were variable and NK activity was unimpaired.

Shuttle Crew Study

A brief summary of some Shuttle studies indicated that a reduction in several T-cell subsets were observed when expanded immunophenotyping assays were performed. Decrease in NK-cells, T inducer and T cytotoxic subsets were seen whereas monocytes increased to a similar magnitude as was observed during OE II. Furthermore, characterizations of these monocytes by flow cytometry indicate a novel population that may be more immature since their expression of insulin and insulin-like growth factor receptors were distinctly different from normal monocytes (4).

U.S. Air Force Academy Cadets

To correlate associations between reduced in vitro T-cell responses and susceptibility to viral illness, during stress, a more homogeneous population was studied at the United States Air Force Academy. Advantages of this study include similar exposure to infectious agents, and the subjects are homogeneous regarding age, social/economic status, intellect, diet, lifestyles. Since all subjects are single and do not have children, they are at a more uniform risk for contracting infectious diseases. They also have excellent health care monitoring, at the cadet clinic and experience major stressors at the same time. Their personality profiles are very similar to astronauts. The negative aspects of this study however, are that it's difficult obtaining low stress control periods with this group of highly and continually stressed individuals, and the findings may not be applicable to the general population. Furthermore, they experience different stress depending on their own unique talents, as some individuals find the academic load most stressful, whereas others find physical or physiological hazing to be more traumatic. The 89 cadets did rate themselves as having significantly more perceived stress as well as a greater response to stress during basic cadet training and this was associated with significant reduction in PHA responsiveness of 20-30% similar to what was observed from Shuttle crews. This in vitro reduction could be prevented by co-culturing cells with IL-2. This reduced proliferative responsiveness did not discriminate between those 63 individuals who remained free of illness and those 27 who had one or more upper respiratory infections during the observation period. Therefore this study did allow us to investigate potential mechanisms of neuro-endocrine mediated stress-induced immune suppression in humans. A strong correlation between reduced immune responsiveness in vitro and susceptibility to viral illnesses was not demonstrated.

Specific areas of investigation to exploit the uniqueness of the Polar environment as a space station analogue should include infectious disease studies which investigate transmission of infectious agents, reactivation of latent viruses, and studies which identify mechanisms of host immunocompetence and susceptibility to viral diseases. Immunologic studies should be interdisciplinary and focus on mechanisms of the daily or seasonal variation in human immune responsiveness and the relation to circadian rhythm. Clinical trials could also be performed in this environment including active immunizations, antiviral chemotherapy, prophylactic regiments or biologic response modifiers. Also, testing potential markers for immunosuppression or cellular dysfunction could be conducted since immune effector cells are readily available from peripheral blood. Endocrine studies should also be done concomitantly to identify potential mechanisms of seasonal variation, differences between women and men in this environment and possibly studying bone mineralization in an environment where stress-induced endocrine responses might be invoked. Additional suggestions to improve the scientific yield from Polar/NASA studies would include more attention to subject selection; include both men and women and match personality and psychosocial features to astronauts likely to travel to the Space Station Freedom, Lunar Colony or Mars. Perhaps subjects could be selected in a nation-wide competition, similar to astronauts to insure a higher quality of subjects who would also agree to not abuse alcohol which could be a major confounding variable in interpreting results of any physiological or cognitive of studies in this isolated, controlled environment. The station physician or PhD investigator could learn the specific assays to be performed during the winter-over period at the PIs lab. The Polar science facilities may require expansion but this would be an ideal environment to verify the use of automated instruments and telecommunication capabilities in a remote laboratory similar to those planned for the Space Station Freedom. It is also recommended that an appropriate control group perhaps remaining at Christchurch, N.Z. be studied simultaneously.

Collaborators for the above studies have included: from NASA/Johnson Space Center; Gerald Taylor, Nitza Cintron, Clarence Sams, Laurie Neale, and Elizabeth Kraus. From the University of Colorado; Morey Smith and Chris Robinson. From the University of Texas Medical Branch at Galveston; Charlie Stuart, Eric Smith, David Lee, Ed Blalock and Russ Gardner. University of Oklahoma; Harold Munchmore and Nan Scott. U.S. Army Research Institute of Environmental Medicine in Natick Massachusetts; Paul Rock, Charlie Houston and Allen Simmermen. U.S. Air Force Academy; Gary Coulter, Paul Sherry, Tom Mabry, Ron Reed and Robert Ginnett.

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Attachment 12